

REMARKS

Claims 1-5, 7-12, and 14-20 are pending in this application. Non-elected claim 12 has been withdrawn from consideration by the Examiner. By this Amendment, the specification and claims 1, 11, and 14-19 are amended and claim 6 is canceled. Support for the amendments to the claims and specification may be found, for example, in the originally filed specification. For example, the amendments to claim 1 are supported by canceled claim 6 and by the specification at page 4, line 33 to page 5, line 2 and at page 8, lines 24-25; the amendments to claim 11 are supported by the specification at page 5, lines 13-14; and the amendment to the specification is supported by the specification at page 8, lines 24-25, page 9, line 30, page 10, line 20, and page 11, line 17 (which consistently describe a heating prior to the emulsification; the previous recitation "the emulsification according to step a)" on page 4, line 33 is a typographical error). No new matter is added.

In view of the foregoing amendments and following remarks, Applicants respectfully request reconsideration and allowance.

I. Claim Objections

The Office Action objects to claims 1-11 and 14-20 for an informality in independent claim 1. By this Amendment, claim 6 is canceled, rendering its objection moot. As to the remaining claims, claim 1 is amended according to the Examiner's helpful suggestion. Accordingly, Applicants respectfully request reconsideration and withdrawal of the objections.

II. 35 U.S.C. §112, Second Paragraph Rejection

The Office Action rejects claims 1-11 and 14-20 as being indefinite under 35 U.S.C. §112, second paragraph. By this Amendment, claim 6 is canceled, rendering its objection moot. As to the remaining claims, claims 1 and 11 are amended to obviate the indefiniteness rejections.

Claim 1 is amended to recite "wherein the aqueous and oil phases are heated to a temperature of from 30°C to 35°C before said emulsification," thus clarifying how cooling can take place. In connection with this amendment, the specification is also amended, as indicated above, to eliminate a typographical error.

In addition, claim 11, from which claim 19 depends, is amended to recite "a peptide chain," thus granting claim 19 antecedent basis to recite "said peptide."

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

III. 35 U.S.C. §103(a) Rejection

A. Higashi, Joscelyne, Moeritz, and Forster

The Office Action rejects claims 1-10 and 14-17 under 35 U.S.C. §103(a) over Higashi et al., *Size of lipid microdroplets effects results of hepatic arterial chemotherapy with an anticancer agent in water-in-oil-in-water emulsion to hepatocellular carcinoma*, 289 J. Pharmacology and Experimental Therapeutics 816-819, no.2 (1999) ("Higashi") in view of Joscelyne et al., *Membrane emulsification-a literature review*, 169 J. Membrane Sci. 107-117 (2000) ("Joscelyne") and DE 19630176 to Moeritz ("Moeritz"), and further in view of Forster et al., *Production of fine disperse and long-term stable oil-in-water emulsion by the phase inversion temperature method*, 13 J. Dispersion Sci. and Tech. 183-193, no.2 (1992) ("Forster"). By this Amendment, claim 6 is canceled, rendering its rejection moot. As to the remaining claims, Applicants respectfully traverse the rejection.

The combination of Higashi, Joscelyne, Moeritz, and Forster would not have rendered obvious the process of claim 1 for at least the following reasons.

1. The Applied References Do Not Teach Or Suggest Step B

The combination of Higashi, Joscelyne, and Moeritz fails not teach or suggest a process as recited in claim 1, including step b), which recites: "emulsifying the aqueous phase by passing the aqueous phase through a largepored, porous membrane into an oil phase, wherein the aqueous and oil phases are heated to a temperature of from 30°C to 35°C before said emulsification."

The Office Action at page 8 acknowledges that Higashi, Joscelyne, and Moeritz fail to teach this feature, but asserts that it would have been obvious to optimize the emulsification conditions. This mere assertion is insufficient to support a *prima facie* case of obviousness. The examiner has provided no support for this assertion. Higashi provides no teaching to modify the temperature in this step, let alone that doing so would optimize the process. Joscelyne, asserted to teach that temperature can be an important parameter, similarly provides no reason to modify the temperature in a process as claimed. The mere fact that a parameter is "important" does not provide motivation. The claimed range of "30°C to 35°C" could not have been extrapolated from the very general asserted teachings. Thus, Joscelyn does not suggest to modify the Higashi process to include feature b) as claimed.

Furthermore, the Office Action fails to establish that the temperature of the phases is a result-effective variable in the process of Higashi and recognized as such in the art. In the absence of such a showing, optimization of such a parameter cannot be asserted to be obvious. Accordingly, the Office Action fails to establish that such a feature would have been *prima facie* obvious in view of the applied references.

As no proper combination of the art suggests step b) as claimed, withdrawal of the rejection is requested.

2. The Applied References Do Not Teach Or Suggest Step C

The combination of Higashi, Joscelyn, and Moeritz also fails to teach or suggest "c) phase inversion of the heated emulsion from b), by cooling the mixture at a cooling rate of at least 0.3 K/min, where an emulsifier is added either to the aqueous phase in a) or to the oil phase in b) or to both phases" as recited in claim 1 for at least the following reasons.

a. Moeritz Does Not Teach or Suggest A Process With One Aqueous Phase

The Office Action acknowledges at page 7 that Higashi and Joscelyne do not teach "phase inversion of the heated emulsion from b), by cooling" as claimed. However, it asserts that Moeritz cures their deficiency. Applicants respectfully disagree.

The phase inversion process described in Moeritz is substantially different from that of claim 1. Moeritz (English-language translation provided herewith ("Translation")) discloses the principle method of transferring an o/w emulsion to a w/o emulsion, and vice versa. *See* Translation at p. 4, lns. 13-21. Moeritz does not, however, disclose a "process for the preparation of ... multiple emulsions of water/oil/water (W/O/W) type" that are produced via "phase inversion" as recited in claim 1. The process of claim 1 results in a w/o/w type emulsion where "the aqueous phase" that contains the active ingredient is found on the outer and inner water phases.

Moeritz does not disclose such a process or end product. In Moeritz, three solutions (A, B, and C) are made. Solution A is an "oily-phase" (comprises significant amounts of oils), solution B is an "aqueous phase" (it is filled up to 100 with water), and solution C is also an "aqueous phase" (it is made from a composition containing 70 wt% water, with no additional oils added thereto). *See id.* at pp. 9-10 (Tables). Thus, Moeritz discloses a process with two distinct aqueous phases.

The process of Moeritz is designed to integrate the three distinct solutions. In the process, solutions A and B are heated to 85°C, then poured together and cooled to 60°C to form a w/o emulsion. *See id.* at p. 12, ln. 25-p. 13, ln. 4. After this, the w/o emulsion is further cooled to 40°C to induce phase inversion to a o/w emulsion. *See id.* at p. 13, lns. 4-5. To the resulting o/w emulsion, solution C is added as a continuous phase resulting in a w/o/w emulsion. *See id.* at p. 13, lns. 5-7.

These steps involving three distinct solutions, two of which are distinct aqueous solutions do not teach or suggest instant step c). Because the outer and inner water phases in Moeritz have distinct compositions, the outer water-phase is not produced from the prior water phase of the w/o emulsion as is the case in instant claim 1. For at least this reason, there is no reason provided by Moeritz to modify the other references as claimed and the combination of applied references would not have rendered obvious claim 1. Therefore, withdrawal and reconsideration are requested.

b. Forster Does Not Teach Or Suggest The Claimed Cooling Rate

In addition to the above-described deficiencies, the combination of references would not have rendered obvious the claimed cooling rate of "at least 0.3 K/min" as recited in step c) of claim 1. The Office Action acknowledges at page 9 that Higashi, Joscelyne, and Moeritz do not teach "a cooling rate of at least 0.3 K/min" as claimed. However, it asserts that Forster cures their deficiency. Applicants respectfully disagree.

Forster neither cures the broader deficiencies of Higashi, Joscelyne, and Moeritz nor their failure to teach or suggest the specific cooling rate. Forster does not, nor is it asserted to teach the specifically claimed cooling rate. It is, however, asserted to support the Office Action's assertion that it would have been obvious for one of ordinary skill in the art to use various

cooling rates. The Examiner has provided no support for this assertion. The fact that the cooling rate in Forster was insignificant has nothing to do with the cooling rate in the process of claim 1. Forster does not teach or suggest, alone or in combination with the other references, how to produce w/o/w emulsions as claimed. The process of Forster is not the same as or even similar to claim 1, and as such, one of ordinary skill in the art would not have modified the already deficient reference combination in view of Forster to yield the claimed process.

Claim 1 would not have been rendered obvious by the combination of Higashi, Joscelyne, Moeritz, and Forster. Claims 2-5, 7-10, and 14-17 depend from claim 1 and, thus, also would not have been rendered obvious by the applied references. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Higashi, Joscelyne, Moeritz, Forster, and Ganne

The Office Action rejects claims 1, 10-11, and 18-20 under 35 U.S.C. §103(a) over Higashi, Joscelyne, Moeritz, Forster, and U.S. Patent No. 6,251,407 to Ganne et al. ("Ganne"). Applicants respectfully traverse the rejection.

The deficiencies of Higashi, Joscelyne, Moeritz, and Forster with respect to claim 1 are described above. Ganne, which is only relied upon by the Office Action for its alleged disclosure of the additional limitations recited in claims 11 and 18-20, at least fails to cure the deficiencies of the combination of Higashi, Joscelyne, Moeritz, and Forster with respect to claim 1. As such, the combination of Higashi, Joscelyne, Moeritz, Forster, and Ganne fails to teach or suggest each and every limitation of claim 1. Accordingly, the subject matter of claim 1 cannot be fairly considered to have been rendered obvious by the combined teachings of Higashi, Joscelyne, Moeritz, Forster, and Ganne.

Claims 11 and 18-20 depend from claim 1 and, thus, require all the limitations of claim 1. Thus, for at least the reasons discussed above, claims 11 and 18-20 would not have been rendered obvious by the combined teachings of Higashi, Joscelyne, Moeritz, Forster, and Ganne.

In addition to the above reasons, claims 11 and 18-20 would not have been obvious for the following additional reasons. The Office Action acknowledges at page 10 that Higashi, Joscelyne, Moeritz, and Forster do not teach an active ingredient that is encompassed by claims 11 and 18-20. Ganne does not cure this deficiency. Although Ganne discloses some emulsions that may be prepared according to conventional methods, Ganne fails to describe the process according to claim 1. One of ordinary skill in the art would therefore have had no reason to assume in view of Ganne, that the specific parameters and steps outlined in claim 1 would be applicable to the compositions described in Ganne. The Office Action asserts that substitution of one active ingredient for another would have been obvious. However, there is no suggestion or teaching to use the actives in Ganne in the process as claimed – especially since Ganne describes a totally different process. Substitution of the active ingredients in different processes would not have been obvious. As such, a *prima facie* case of obviousness has not been established with respect to claims 11 and 18-20.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Rejoinder

Applicants also respectfully request rejoinder of non-elected claim 12. This application is subject to unity of invention practice as set forth in PCT Rule 13. *See* MPEP §1893.03(d). There is no lack of unity of invention between claim 1 and withdrawn claim 12. In fact, claim 12 depends from claim 1 and, thus includes all the limitations of claim 1. For at least the reasons

presented above, claim 1 is believed to be patentable. Accordingly, dependent claim 12 is also believed to be patentable. Applicants respectfully request withdrawal of the Restriction Requirement and rejoinder of claim 12.

V. Conclusion

In view of the foregoing, Applicants respectfully submit that this application is in condition for allowance. Applicants earnestly solicit favorable reconsideration and prompt allowance of the application.

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Should the Examiner believe that anything further would be desirable to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below. Applicants authorize the Commissioner to charge Deposit Account No. 50-4254, referencing Attorney Docket No. 2901652-000004 for fees due or any deficiencies of fees and to credit any overpayments.

Respectfully submitted,

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Attachment:
English-Language Translation of Moeritz

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